ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

1953

243 CHARLES STREET

BOSTON, MASSACHUSETTS

STAFF

David G. Cogan, M.D.: *Associate Professor of Ophthalmic Research — Director*

W. Morton Grant, M.D.: *Assistant Professor of Ophthalmic Research*

David D. Donaldson, M.D.: *Instructor in Ophthalmic Research*

Jin H. Kinoshita, Ph.D.: *Instructor in Biochemistry*

Robert R. Trotter, M.D.: *Instructor in Ophthalmic Research*

Toichiro Kuwabara, M.D.: *Assistant in Ophthalmic Research*

Harold L. Kern, Sc.D.: *Assistant in Ophthalmic Research*

FOR more than two decades the Howe Laboratory has carried on diverse activities, comprehensively called ophthalmic research. With roots spreading into the clinical and basic sciences, the Laboratory has had an unparalleled opportunity, and challenge, to study the eye in health and disease. Its contributions have ranged from the development of diagnostic and therapeutic procedures to the establishment of fundamental data of a purely scientific nature. The past year has been no exception, with investigations that have included glaucoma, neuro-ophthalmology, toxicology, biochemistry and histochemistry of ocular tissues.

Research Activities

The outstanding contributions of Drs. Grant and Paul A. Chandler, and more recently of Dr. Trotter, have established a firm basis for the understanding of glaucoma and a tentative program for its effective control. The large number of "tonographic stations" set up throughout the country and abroad in accordance with Dr. Grant's pilot model at the Howe Laboratory attest to the practical consequences of these investigations. At present an extensive program is being carried out in comparing tonographic measurements (1) with the results of certain provocative tests for glaucoma, (2) with the various types of glaucoma, and (3) with the responses to surgical procedures. Specifically, the so-called water-drinking test has shown a good correlation in "open angle" glaucoma between the rise in intraocular pressure and the resistance to aqueous outflow as measured by tonography. With the "angle closure" glaucoma the rise in intraocular pressure has been found to be due to a bulging of the iris against the trabeculum and consequent obstruction to outflow of aqueous humor. Peripheral iridectomy with tight closure of the wound has proved to be effective and specific in relieving this latter type of glaucoma. This operation is much safer than many of the non-specific filtration procedures which have been often employed in the past through lack of understanding of the underlying mechanism.

The most interesting medical treatment for glaucoma which has been under investigation is that using the carbonic anhydrase inhibitor Diamox. A study of the effects of this substance on glaucomatous patients was undertaken after experimental studies in rabbits had shown a lowering of the intraocular pressure. The original interest in carbonic anhydrase inhibition stemmed from Friedenwald's hypothesis of secretion of bicarbonate for the maintenance of the osmotic pressure of the aqueous humor and the subsequent demonstration by Kinsey of an actual excess of bicarbonate in the aqueous humor (compared with the plasma). On the assumption that the enzyme, carbonic anhydrase, might be involved in the transfer of carbon dioxide from the blood to aqueous, it appeared reasonable that inhibition of the enzyme might decrease the rate of aqueous humor formation and thereby lower the intraocular pressure. Diamox appears to be safe for daily oral administration, and preliminary trial on glaucomatous volunteers has given promising results.

Fundamental biochemical studies on the eye continue to occupy a prominent position in the Howe Laboratory. One important study has aimed at determining the reactions from which energy is derived in maintaining the normal metabolism and transparency of the lens. Dr. Kineshita's experiments with the use of radioactive isotopes have indicated that the lens relies primarily on anaerobic glycolysis for the production of its energy. This is further borne out by the finding that the lens cannot oxidize pyruvic acid to carbon dioxide to any significant degree, as it would do if there were an active aerobic mechanism.

Studies on the corneal epithelium have revealed that the utilization of glucose may be through a metabolic cycle other than the universally accepted glycolytic pathway. The alternate metabolic cycle consists of three main stages: (1) the two-step oxidation of glucose-6-phosphate to ribose-5-phosphate and carbon dioxide; (2) the conversion of ribose-5-phosphate to sedoheptulose phosphate, a seven carbon sugar; and (3) the resynthesis of glucose-6-phosphate from sedoheptulose phosphate. The various steps of this cycle have been demonstrated in homogenates of the corneal epithelium. This pathway allows the corneal epithelium to oxidize glucose directly without the intervention of the Krebs citric acid cycle and appears to be the simplest means by which carbohydrates may be metabolized. Whether this is the major pathway for carbohydrate metabolism in the corneal epithelium and just how important a role it plays in the physiology of the cornea are facts yet to be determined.

The study of fat deposition in the cornea, being currently pursued by Drs. Kuwabara and Cogan, has a twofold stimulus. In the first place it is felt that the mechanism with which fat is laid down in the cornea in human beings has not received the experimental attention which its practical importance warrants. Secondly, it is hoped that an understanding of the mechanism in the cornea will yield crucial information on the wider problem of fat accumulation in blood vessels and other tissues of the body. There is a strikingly suggestive analogy in the formation of arcus senilis in human beings and the development of atheroma in arteriosclerosis. Both occur predominantly with age and consist simply of the deposition of fat. The cornea which offers unique opportunities for making observations during life gives promise of providing much needed data on the factors involved in the deposition and removal of fat from the eye and elsewhere in the body.

Chemical injuries to the cornea have occupied a prominent place on the agenda of the past year under the direction of Drs. Grant and Kern. The prime aim has been a determination of the chemical and physical basis for injury and opacification of the cornea by alkalies. The degree of injury appears to be correlated with cation binding by certain amino acids of the constituent tissue of the cornea. Such studies as these form the necessary basis for the future treatment of chemical injuries.

SERVICE FUNCTIONS

In a laboratory situated within the walls of a hospital, dedicated to the ultimate understanding of disease processes in patients, there can be no sharp division between research activities and service functions. Although the administrative set-up of the Howe Laboratory happily prevents the encumbrance of the research operations by routine functions, there is nevertheless considerable moral obligation to initiate certain services and sometimes to maintain them. This is not wholly undesirable for, within limits, the advantages are mutual.

A noteworthy service function is photography. Dr. Donaldson who has so ingeniously advanced photography of the eye has now rejoined the Howe Laboratory after completing his ophthalmic residency. The collection of stereophotographs which he has made comprises an extremely valuable reservoir of clinical conditions that has attracted a wide group of students to the Laboratory. They are undoubtedly the best photographs of their kind in the world. Because of the demand for teaching material a separate set of photographs has been set aside for loan purposes.

The service functions of tonography have threatened to be a Juggernaut. The constant stream of patients referred to the Laboratory for glaucoma evaluation has impeded to some extent the more basic researches. Accordingly, space is being solicited nearer the Clinic where the measurements, supervised by Dr. Trotter, may be carried on outside the Laboratory.

The Laboratory personnel takes pride and profit in serving a consultative function for a variety of interests inside and outside the hospital and medical school. The especially intimate association with the Department of Neurology has resulted in several neuro-ophthalmic studies (ocular motor apraxia, ocular motor dysmetria, ocular signs of Wernicke's encephalopathy, and survey of spasmus nutans) and neuroanatomic preparations. Demonstrations of the eye structure have been prepared for the Museum of Science. The Laboratory assisted in setting up experiments for the U. S. Air Force aimed at obtaining data on the radiation hazards to the eye.

Teaching activities are a service function that need no annual enumeration. However, it may be mentioned that Dr. Cogan was one of the international team of six ophthalmologists sent by the World Health Organization to Cairo for the purpose of conducting a two-week seminar in connection with the Golden Jubilee Meeting of the Egyptian Ophthalmological Society.

The Howe Library continues to be an active point of reference as indicated by the more than 6,000 reader visits during the past year. The initiative and energy of its director, Mr. Charles Snyder, have made it a model of serviceability. Its growth has been in healthy accord with that of the research and teaching functions with which it is allied.

These are a few of the fringe activities conducted by the Laboratory staff during the past year. In the aggregate they and others not mentioned have occupied a considerable part of the Laboratory's activities.

Organization

The guiding philosophy of the Howe Laboratory is akin to that expressed by President Conant in his final Report for the University as a whole: "Solvency for a university depends on far more than balancing the dollar budget each year. . . . Solvency depends on a stable personnel policy." Our first aim has been to obtain talent with those intangible assets of curiosity, imagination, and integrity. Our second aim has been to provide facilities where that talent can be expended with the greatest vigor and enterprise. To both ends we have been immeasurably assisted by a corps of friends and counsellors, both within and without the profession. There is no denying, however, that the limitations of space and income have made us fall far short of our hopes and have incurred numerous specific difficulties for all members of the staff. It is therefore an exciting prospect to contemplate new laboratory quarters in the near future where some expansion and more efficient operation will be possible. If, then, additional endowment may be obtained the possibilities for future developments in ophthalmic research at the Howe Laboratory will be bright indeed.

As has been the occasional custom in the past, a letter has been recovered from the files of the past year and is reprinted here to convey the day-to-day thinking of the Laboratory. The last letter was to the Dean of the Harvard Medical School. The present letter is also to a person who has been most helpful in the administrative affairs of the Laboratory, Mr. Henry H. Meyer, Chairman of the Board of Trustees of the Massachusetts Eye and Ear Infirmary.

July 8, 1953

MR. HENRY H. MEYER
243 Charles Street
Boston 14, Massachusetts

DEAR MR. MEYER:

The mission of the Howe Laboratory, as I see it, is in part to solve, or attempt to solve, specific problems in the general area of prevention of blindness and in part to indoctrinate selected scientists with the humane and intellectual advantages of a career in ophthalmic research. Of the two the latter probably has the more far-reaching consequences, for the problems will take care of themselves once that the personnel is available. Yet it is for this phase of our function that support is most difficult to find. And it is costly if one feels, as I do, the necessity of obtaining first-rate investigators and maintaining them with the facilities and dignity comparable to that in the academic departments from which they have come. A conservative estimate (salary, equipment, and supplies) would be of the order of $12,000 a year per investigator.

With our limited fixed income of less than $40,000 annually, we can scarcely support an adequate program. Nor are the funds for projects or junior fellowships suitable for this type of development where one must think in terms of at least ten-year tenures.

It is my persistent hope that one of the foundations with imagination and experience (and resources!) will realize the importance of this type of development. If it were possible to obtain additional support for bringing in outside talent, this Laboratory would pledge itself to pursue the operational aspect with the same enthusiasm and conscience that has characterized its quarter century of existence to date. By now, we have had, I believe, a reasonable measure of experience in those intangibles that make for the selection and development of career investigators for ophthalmic research.

Sincerely,

DAVID G. COGAN, M.D.

Too much cannot be said in appreciation of the many contributions to the Laboratory during the past year. To the following persons and organizations we are particularly grateful for their support.

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For studies on tonography and toxicology of the eye:
For studies of eyes in identical and fraternal twins:

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For studies on radiation cataracts:
For studies on metabolism of the ocular lens:

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For studies on intraocular fluids:

The Snyder Foundation

For studies on fat metabolism in the cornea and aging processes as reflected in the cornea:

Boston Eye Bank
The Massachusetts Heart Association
The American Heart Association

For studies on retinal degenerative disease:

Mrs. Bessie Greenwald

For the support of the Howe Library of Ophthalmology:

Elizabeth M. Howe Bequest

David G. Cogan, M.D.
Director

LECTURES — 1953

Cogan, D. G.

Lesions of the eye from radiant energy. Golden Jubilee Meeting of the Egyptian Ophthalmological Society, in Cairo, Egypt, February, 1953.

Clinical physiology of the cornea. Golden Jubilee Meeting of the Egyptian Ophthalmological Society, in Cairo, Egypt, February, 1953.

The ocular effects of atomic radiation. Regional Meeting of the Association of Surgeons of East Africa, in Nairobi, East Africa, March 3, 1953.

Retinal vascular disease. Postgraduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, April 22, 1953.

with Adams, R. D. A type of conjugate gaze paralysis (ocular motor apraxia). Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 15, 1953.

Ophthalmological findings in neurological conditions. Veterans Administration Hospital, in Rutland Heights, Massachusetts, April 24, 1953.

with Victor, M. Ocular findings in Wernicke's encephalopathy. American Ophthalmological Society Meeting, in Hot Springs, Virginia, May 28, 1953.

Ocular dysmetria, flutter-like oscillations of the eyes and opsoclonus. Section on Ophthalmology, American Medical Association, New York City, New York, June 2, 1953.

Some common eye disorders in older people. Medical Symposium under the joint auspices of the Maryland Academy of General Practice and Lederle Laboratories, in Ocean City, Maryland, September 12, 1953.

Neuro-Ophthalmic Syndromes: Internuclear ophthalmoplegia, spasm of near reflex, and platybasia. Lesions of the corneal stroma. Lectures presented at the Joint Meeting of the North Carolina Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology, in Charleston, South Carolina, September, 1953.

Dizziness as a symptom of ocular disturbances. Discussion as part of panel on "The Dizzy Patient" at the Joint Meeting of the North Carolina Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology, in Charleston, South Carolina, September 16, 1953.

Ophthalmic manifestations in the neurological patient. Connecticut Postgraduate Seminar in Psychiatry and Neurology, sponsored jointly by the Department of Psychiatry of Yale University School of Medicine and the Joint Committee of State Mental Hospitals, Fitkin Amphitheatre, Yale University School of Medicine, in New Haven, Connecticut, October 14, 1953.

House Officer Lectures, Massachusetts Eye and Ear Infirmary.

Corneal dystrophies.	October 13, 1953.
Visual pathways.	December 29, 1953.

DONALDSON, D. D.

Follow-up studies on rabbits exposed to low doses of x-rays. Fourth Conference on Radiation Cataracts, National Research Council, in Washington, D. C., February 28, 1953.

Lens opacities. House Officer Lecture, Massachusetts Eye and Ear Infirmary, October 6, 1953.

GRANT, W. M.

with Trotter, R. R. Open-angle glaucoma. Philadelphia College of Physicians, January 15, 1953.

Action of drugs in treatment of glaucoma. Harvard Medical School Department of Pharmacology, February 26, 1953.

Glaucoma and the angle. Detroit Ophthalmological Society, March 26, 1953.

Lime burns of the eye and their treatment with EDTA. Syracuse Eye and Ear Club, April 8, 1953.

Experimental studies on the outflow of aqueous humor. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 15, 1953.

Lectures on Toxicology and Tonography in Lancaster Courses in Ophthalmology, in Waterville, Maine, August 31 and September 1, 1953.

TROTTER, R. R.

Ophthalmic survey in Ryukyu Islands. New England Ophthalmological Society, in Boston, Massachusetts, February 18, 1953.

with Grant, W. M. Follow-up of peripheral iridectomy in angle-closure glaucoma. New England Ophthalmological Society, in Boston, Massachusetts, April 14, 1953.

Ophthalmic emergencies in industry. Assembly of nurses from industrial plants in greater Boston at Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, June 25, 1953.

Glaucoma. Graduate Nursing Students at Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, September 29, 1953.

PUBLICATIONS — 1953

Cogan, D. G.

A type of congenital ocular motor apraxia presenting jerky head movements. Jackson Memorial Lecture. Am. J. Ophth. 36: 433–441, April, 1953.

with Dreisler, K. K. Minimal amount of x-ray exposure causing lens opacities in the human eye. Arch. Ophth. 50: 30–34, July, 1953.

with Adams, R. D. A type of paralysis of conjugate gaze (ocular motor apraxia). Arch. Ophth. 50: 434–442, October, 1953.

with Donaldson, D. D., Goff, J. L. and Graves, E. Experimental radiation cataract. III. Further experimental studies on x-ray and neutron irradiation of the lens. Arch. Ophth. 50: 597–602, November, 1953.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology .... Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.